UNITED STATES DEPARTMENT OF COMMERCE
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/495,448	01/31/00	LAU	L 287758/36072

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KATTEN, MUCHIN & ZAVIS
525 WEST MONROE STREET
SUITE 1600
CHICAGO IL 60664-3693

EXAMINER	
BRUMBACK, B	
ART UNIT	**PAPER NUMBER**
1642	10

DATE MAILED: 08/29/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/495,448	Lau
Examiner	**Art Unit**
Brenda Brumback	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

P riod for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 20, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above, claim(s) *1-3 and 9-23* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *4-8* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 6
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Election/Restriction

2. Applicant's election with traverse of Group II, claims 4-8, in Paper No. 8 is acknowledged. The traversal is on the ground(s) that all of the pending claims have the unifying characteristic of involvement of an ECM signaling molecule-related biomaterial such as Cyr61 and that this unifying characteristic is not reconcilable with a restriction requirement predicated on MPEP 806.04. This is not found persuasive because although applicant asserts that all of the claims involve an ECM signaling molecule-related biomaterial, the biomaterials recited in the different groups are not the same and would thus require separate and distinct searches for each of the recited groups. Furthermore, the methods of Groups I-VII have different method steps, utilize different components, have different outcomes, and are for different purposes. For these reasons the groups are not unified and examination of all of the groups would constitute a serious burden.

The requirement is still deemed proper and is therefore made FINAL.

3. Pending claims are 1-23. Claims 1-3 and 5-23 are withdrawn from consideration as directed to a nonelected invention. Claims 4-8 are pending and under examination.

Information Disclosure Statement

4. The Information Disclosure Statement filed 01/19/01 has been considered. A signed copy is attached hereto.

Specification

5. The use of the trademarks MAXBAC®, MATRIGEL®, HYDRON®, SEPHACRYL®, SEPHAROSE®, PHOSPHORIMAGER®, ROBOCYCLER®, HEMO-DC®, IMMULON®, REMOVAWELL®, and TRITON® has been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

6. Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 5 recites fibroblast cells comprising an $\alpha_6\beta_1$ integrin; however, claim 4 from which claim 5 depends, also recites this

limitation. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form

Claim Rejections - 35 USC § 112

7. Claims 5, 6, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6 recite the limitation "said first and second fibroblast cells" in lines 1-2. There is insufficient antecedent basis for this limitation in the claims because claim 4, from which the claims depend does not recite first and second fibroblast cells. Correction is required.

Claim 8 contains the trademark/trade name MATRIGEL® . Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe and, accordingly, the identification/description is indefinite.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4 -8 rejected under 35 U.S.C. 103(a) as being unpatentable over Iwamoto et al. (Advances in Experimental Medicine and Biology, 324:141-9, 1992) in view of either Yang G.P., Dissertation Abstracts International, 54/8:DA9335171, February 1994) or O'Brien et al. (Cell Growth and Differentiation, 3:645-654, September 1992) and Bork, P., FEBS Letters, 327/2:125-130, 1993) and Lin et al. (Cancer Research 53:2950-2953, July 1993).

The claimed invention is drawn to a method of screening for a modulator of cell migration comprising forming test and control gel matrices of Cyr61; a suspected modulator of cell migration; and one of MATRIGEL®, collagen, or fibrin; seeding human fibroblast cells presenting $\alpha_6\beta_1$ integrin onto the test and control gel matrices; incubating the fibroblast cells; measuring the levels of cell migration in the test and control matrices by visual inspection; and comparing the levels of cell migration, whereby a modulator of cell migration is identified by its ability to alter the level of cell migration in the test matrix compared to the control matrix.

Iwamoto et al. teach a method of screening for a modulator or inhibitor of cell migration or invasion comprising forming test and control gel matrices of MATRIGEL® (which comprises

collagen), layering normal MRC-5 human (or mouse) fibroblast cells (normal control gels) and malignant human tumor cells (test gels) onto the matrices, incubating the cells, and measuring the levels of cell migration by microscopic inspection. Iwamoto et al teach utilization of the assay for testing for factors which inhibit tumor cell migration *in vitro* as a screen for compounds with the potential to inhibit tumor cell invasion *in vivo* (see page 141, abstract; page 142, second paragraph; the paragraph bridging pages 142-143; and page 143, second full paragraph). Iwamoto et al. teach that Cyr61 interacts with heparan sulfated proteoglycans on the cell. Iwamoto et al. teach adding a chemoattractant to the test system (page 143, second full paragraph), but do not teach the chemoattractant as Cyr61. Iwamoto et al. also do not teach the human fibroblast cells as presenting $\alpha_6\beta_1$ integrin or as comprising a heparan sulfate proteoglycan.

Yang teaches the *cyr61* is a member of the family of immediate early genes which transcribes Cyr61, a member of a family of proteins known to be chemoattractants, mitogens and proto-oncoproteins. Yang teaches that Cyr61 has chemoattractant activity.

O'Brien et al. teach that *cyr61* is a growth factor-inducible immediate early gene which encodes a member of a family of growth factors comprising Cyr61, Fisp12, and CTGF. O'Brien et al. teach that CTGF, one of the members of the family, possesses mitogenic and chemotactic activities (see page 645, the abstract and first three paragraphs). O'Brien teaches that Cyr61 interacts with the cell surface and the extracellular matrix through interactions with heparan sulfate proteoglycans. Bork teaches that all of the members of the family of growth regulators comprising CTGF, Fis12, and Cyr61 have most of their molecular functions in common and that

functional information provided for one member can be transferred to other proteins of the family (see page 125, the abstract, and page 126, first full paragraph). Thus, Bork suggests that the chemoattractant function described by O'Brien for CTGF can be also attributed to Cyr61.

Lin et al. teaches that $\alpha_6\beta_1$ integrin is abundantly expressed in all neoplastically transformed fibroblast cell lines but not in normal fibroblasts (see page 2950, the abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have used Cyr61 as an alternative chemoattractant in the cell invasion assay taught by Iwamoto et al., in order to be able to apply the assay to screen for compounds which inhibit the migration of neoplastically transformed fibroblast cells because both Yang and O'Brien with Bork teach that Cyr61 is a chemoattractant which interacts with heparan sulfate proteoglycans on the cell and Lin et al. teach that neoplastically transformed fibroblast cells abundantly express $\alpha_6\beta_1$ integrin. One of ordinary skill in the art at the time the invention was made would have been motivated to do so in order to be able to efficiently screen for tumors of fibroblast derivation.

Conclusion

9.. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Felch et al. (Regional Immunology, 4:363-370, 1992) teach that lung fibroblasts which differentially express $\alpha_6\beta_1$ integrin differ from fibroblasts which do not express $\alpha_6\beta_1$ integrin in their ability to react to proinflammatory cytokines. Felch et al. teach that such fibroblasts are able to migrate in response to chemotactic factors, adhere, and proliferate (see page 369, last sentence).

Mackinnon et al. (Invasion Metastasis, 12:241-252, 1992) teach a cell invasion assay utilizing MATRIGEL® and fibroblast cells.

10. No claims are allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Art Unit 1642 FAX telephone number is (703)-305-3014. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

BB
August 21, 2001

Brenda Brumback
Brenda Brumback,
Patent Examiner